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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,550	12/09/2003	Ole Isacson	25429/9	4567

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EXAMINER	
BOWMAN, AMY HUDSON	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 10/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/731,550	ISACSON ET AL.	
	Examiner	Art Unit	
	Amy H. Bowman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-46* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-16, drawn to a method of generating dopaminergic neurons, wherein a pathway component is inhibited by gene knockout of the nucleic acid encoding said component, classified in class 435, subclass 91.1. **Election of this group requires a further election of species as explained below.**

II. Claims 1-15 and 17, drawn to a method of generating dopaminergic neurons, wherein a pathway component is inhibited by overexpressing small interfering RNA complementary to the mRNA encoding said component, classified in class 435, subclass 91.1. **Election of this group requires a further election of species as explained below.**

III. Claims 1-15 and 18, drawn to a method of generating dopaminergic neurons, wherein a pathway component is inhibited by overexpressing antisense oligonucleotide of the nucleic acid encoding said component, classified in class 435, subclass 91.1. **Election of this group requires a further election of species as explained below.**

IV. Claims 1-15 and 19, drawn to a method of generating dopaminergic neurons, wherein a pathway component is inhibited by contacting the pluripotent cells with antibodies that specifically bind to the pathway

component, classified in class 435, subclass 91.1. **Election of this group requires a further election of species as explained below.**

V. Claims 1-15 and 20, drawn to a method of generating dopaminergic neurons, wherein a pathway component is inhibited by overexpressing a dominant negative version of the pathway component, classified in class 435, subclass 91.1. **Election of this group requires a further election of species as explained below.**

VI. Claims 21-38, drawn to a method for treating a neurodegenerative disease in a patient, wherein a pathway component is inhibited by gene knockout of the nucleic acid encoding said component, classified in class 514, subclass 44. **Election of this group requires a further election of species as explained below.**

VII. Claims 39-42 and 44-46, drawn to an isolated mammalian pluripotent cell expressing a recombinant cell fate-inducing polypeptide having a functional disruption as a result of a homozygous deletion of a gene encoding TGF-β signaling pathway, classified in class 530, subclass 300. **Election of this group requires a further election of species as explained below.**

VIII. Claims 39-41, and 43-46, drawn to an isolated mammalian pluripotent cell expressing a recombinant cell fate-inducing polypeptide having a functional disruption as a result of a missense mutation in a gene encoding TGF-β signaling pathway, classified in class 530, subclass 300.

Election of this group requires a further election of species as explained below.

The inventions are distinct, each from the other because of the following reasons:

The inventions of groups I-V are each directed to related processes. The related inventions are distinct if the (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the inventions as claimed are each drawn to a method for generating dopaminergic neurons comprising overexpressing cell fate-inducing polypeptides, however each method is directed to inhibiting a pathway component by a separate and distinct mechanism. Each of the claimed mechanisms involves separate and distinct method steps that are not a consideration of any of the other methods. Therefore, although each of the inventions is drawn to a method of generating dopaminergic neurons, each method is considered unrelated because each method is carried out by a different mechanism. Specifically, gene knockout of the nucleic acid encoding a component, overexpression of siRNAs, overexpression of antisense oligonucleotides, contact with antibodies, and overexpression of a dominant negative version of a component would each require a separate and distinct search and examination based on the distinct structure and mechanism of each. Therefore, to search for more than one of the inventions would produce an undue search and examination burden.

The inventions of groups I-V are each unrelated to the invention of group VI. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are drawn to separate and distinct methods. The methods of groups I-V have completely different method steps from the method of treatment of group VI and do not involve any consideration of treatment effects. The method of group VI is directed to transplanting dopaminergic neurons into the brain of a patient, which is not a consideration of groups I-V. The methods have different designs, modes of operation, and effects. Therefore, to search for more than one of the inventions would produce an undue search and examination burden.

The inventions of groups I-VI are each unrelated to the inventions of groups VII and VIII. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the inventions of groups I-VI are drawn to methods that have distinct steps that are not directed to the isolated mammalian pluripotent cell of group VII or VIII. The inventions have not been disclosed as capable of use together and have different designs. Therefore, to search for more than one of the inventions would produce an undue search and examination burden.

Inventions of groups VII and VIII are directed to related products. The related inventions are distinct if the (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect;

(2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the inventions as claimed are each directed to isolated mammalian pluripotent cells expressing a recombinant cell fate-inducing polypeptide and having a functional disruption of a TGF-β signaling pathway component, however the functional disruption of each of the groups is caused by a separate and distinct mechanism that would require a separate and distinct search and examination. A search for a functional disruption that is specifically a result of a homozygous deletion of a gene encoding a TGF-β signaling pathway component would not necessarily return art against a functional disruption that is specifically a result of a missense mutation in a gene encoding a TGF-β signaling pathway component. As instantly claimed, each of the functional disruptions are separate and distinct based on the mechanism. Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

This application contains claims directed to the following patentably distinct species: Nurr-1, PTX3, or Nurr-1 and PTX3 together. Each of the cell fate-inducing polypeptides is structurally and functionally distinct. To search for one of the cell fate-

inducing polypeptides alone would not necessarily return art against the other cell fate-inducing polypeptide or the combination of cell fate-inducing polypeptides.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, Nurr-1, PTX3, or Nurr-1 and PTX3 together, for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

This application contains claims directed to the following patentably distinct species: human cells, mouse cells, rat cells, porcine cells, or non-human primate cells. The species are independent or distinct because each of the types of cells of claims 6, 7, 28, and 29 are completely distinct. A method involving inhibiting one or more pathway components in the cells would be unique to the type of cells being used.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

This application contains claims directed to the following patentably distinct species of pathways and pathway components of claims 9-14, 31-36 and 44-46: Nodal signaling pathway, Activin signaling pathway, BMP2, BMP4, or BMP7 signaling pathway; pathway components selected from the group consisting of Nodal, Cryptic, Cripto, Activin, Activin receptor I, Activin receptor II, Activin receptor IIb, TGF-β receptor, ALK-1, ALK-2, ALK-3, ALK-4, ALK-6, ALK-7, BMP2, BMP4, BMP7, BMPRIa, BMPRIb, BMPRII, Smad2, Smad3, Smad4, Smad5 and Smad6. The species are independent or

distinct because each of the pathways are distinct and contain distinct components based on the pathway. Each pathway involves completely unique structural considerations and would therefore require a separate and distinct search and examination.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed signaling pathway and a signaling pathway component for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. The signaling pathway component must be consistent with the elected signaling pathway.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the

requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103 (a) of the other invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy H. Bowman whose telephone number is (571) 272-0755.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AHB

JD Schultz

JAMES SCHULTZ, PH.D.
PRIMARY EXAMINER